Stages of Change for Adherence to Antiretroviral Medications

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Abstract

Providers do not predict reliably which of their HIV-positive patients are having difficulty adhering to antiretroviral therapy (ART). The transtheoretical, or stages of change model, may be a useful tool to help providers identify patients who are having difficulty with ART adherence. The objective of the current study was to determine the relationship between stages of change and ART adherence among patients who were actively taking ART. Data from a randomized trial of a provider-focused intervention were used to examine the relationship between the stages of change and adherence, measured using electronic monitoring devices in the 30 days following the stages of change assessment. Individuals were eligible for inclusion if they were taking ART and had detectable plasma viral load (HIV-RNA). Repeated measures analysis of covariance was used to determine the impact of stages of change on adherence after controlling for potential confounders. The sample of 137 participants was 22% female, 48% white, 28% African-American, with a mean age of 42 years. Fifty-eight percent reported sex with a man as an HIV risk factor, while 13% reported sex with a woman, 14% reported injecting drugs and 15% reported other risk factors. In adjusted models, those in earlier stages of change (i.e., contemplation and preparation) had significantly lower adherence (-9.8%, $p=0.04$) compared to those in the action and maintenance phases. No demographic characteristics predicted adherence. The stages of change model may function as a screening tool for clinicians to discover patients at-risk of lower adherence.

Introduction

ADHERENCE TO ANTIRETROVIRAL THERAPY (ART) is the strongest predictor of viral suppression for patients with HIV.¹ Unfortunately, adherence among many patients is not optimal, potentially resulting in more rapid disease progression, deteriorating health, and drug resistance. Interventions to improve adherence are urgently needed. To maximize impact, interventions should be targeted to patients with the most difficulty adhering to ART. Research has consistently demonstrated, however, that clinicians are unable to predict non-adherence among patients taking ART.² Self-reported adherence may be subject to social desirability bias, particularly among those not new to treatment. Electronic and biological monitoring strategies can be costly and waiting for treatment failure represents a lost opportunity for intervention. Additional tools are needed so that clinicians can screen patients in order to appropriately target adherence interventions.

Originally developed to characterize behavior changes in the context of smoking cessation³ and widely applied to other behaviors, the transtheoretical, or stages of change, model has also been applied to understanding medication adherence.⁴ The stages of change model describes the progression of cognitions and strategies adopted by individuals as they change behaviors and includes the following phases: pre-contemplation (not considering changing behavior in the next 6 months), contemplation (considering changing behavior in the next 6 months), planning (planning on changing behavior in the next 6 months), action (currently changing behavior), and maintenance (successful behavior change in the past 6 months).⁵ Measures of the stages of change have been validated among patients newly initiating ART,⁶ and have also been shown to predict viral load prospectively in a small sample of HIV positive women.⁷ However, it is unknown how the stages of change relate to adherence over time among patients already taking ART. The objective of the current study, therefore, was to examine the relationship between

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phase in the stages of change and future medication adherence in a diverse sample of patients currently taking ART.

Methods

Data for the current study come from a randomized controlled trial of an intervention that provided short adherence reports at routine visits to clinicians in order to increase patient adherence through improved dialogue about adherence behaviors. Details about the study are provided elsewhere.⁸ Briefly, patients were recruited from two academic medical centers, a community health center, a general medicine practice, and a private infectious disease practice in the New England area. Eligibility requirements included current use of ART, detectable plasma viral load (HIV-RNA) at the most recent clinical visit, willingness to use an electronic pill bottle cap for monitoring ART use, and fluency in English. Enrollment occurred between November 2002 and January 2005. Participation in the RCT included a baseline visit and five additional visits, with randomization occurring at the third visit. Data presented here includes socio-demographic and other patient characteristics, stages of change, and adherence data assessed during each study visit following randomization. The intervention treatment assignment was ignored in this analysis, since it was found to have no effect on adherence.⁸

Socio-demographic, behavioral, and health-related information was assessed using interviewer-administered surveys. Demographic information collected included sex, age, race/ethnicity, highest educational attainment, marital status, homelessness, current employment, and health insurance information (i.e., receipt of Medicaid, MassHealth, Medicare, private medical insurance, free care, or Health Net). Additional information was collected regarding risk behaviors including frequency of alcohol in the prior 30 days, drug use history (i.e., cocaine, heroin, amphetamines, Ecstasy, G, K, or methadone), and HIV acquisition risk factors (i.e., sex with a man, sex with a woman, injection drug use, other). Physical and mental health status were assessed using the Medical Outcomes Study Short Form 12-item (SF-12) survey,⁹ a one-item assessment regarding self-perceived health in general (i.e., excellent, very good, good, fair, poor), and the Primary Care Screener for Affective Disorder (PC-SAD).¹⁰ Finally, information was collected from patients regarding the length of the relationship with their current HIV care provider (e.g., "How long has your current HIV care provider been your provider?").

Adherence was measured on one medication using the Medication Event Monitoring System (MEMS), a system that records the date and the time of each bottle opening. We limited monitoring to daily or twice daily regimens. The medication within the regimen was selected for monitoring according to the following prioritization: protease-inhibitors (PI) over non-nucleoside reverse transcriptase inhibitors (NNRTIs) and NNRTIs over NRTIs. In order to examine future adherence with respect to the stages of change, adherence data were summarized from the 30 days following a study visit. Adherence was summarized as covered time, calculated as the percent of the time in an interval that was covered by medication. Uncovered time began accumulating in the interval 3 h following the expected next dose (i.e., 27 h for once a day medication and 15 h for twice a day). Adherence was

calculated as the total minutes in the 30 days following a study visit minus the number of uncovered minutes in the same interval, divided by the total minutes in the interval $\times 100$. Information regarding ART was also collected from participants and included the type of medication being monitored, the dosing regimen (once or twice daily), the duration of time that the patient had been taking the monitored medicine, and the duration the patient had been taking HIV medications.

Stages of change were assessed at each study visit following randomization with two previously validated survey items.⁶ The first question asked patients to endorse which statement best described how they currently felt about taking ART medications. The statements served to classify patients into the appropriate stage and included: "I do not take and right now am not considering taking my ART as directed" (those endorsing this statement were considered pre-contemplation); "I do not take but right now am considering taking my ART as directed" (classified as contemplation); "I do not take but am planning to start taking my ART as directed" (classified as planning); and "Right now I consistently take my ART as directed." If patients endorsed the last statement, they were asked a second question regarding for how long they had been consistently taking ART as directed. If they reported having done so for less than 6 months, they were classified as being in the action phase, while those classified in the maintenance phase reported having done so for 6 months or longer.

Statistical analysis

The unit of analysis in this study was the study visit. Standard descriptive statistics were used to characterize the sample, investigate the frequency of each phase in the stages of change, and describe adherence over time. Repeated measures ANCOVA (Analysis of Covariance) using an unstructured covariance matrix was used to examine the effect of stage of change on adherence while controlling for socio-demographic characteristics, behaviors, and the health status of patients. Adherence was modeled as a continuous variable ranging from 1 to 100. Initially stages of change were included as a dummy variable with each stage representing a separate category. However, because we were interested in understanding the differences between those who reported consistently taking their medications (action and maintenance) and those who did not (pre-contemplation, contemplation, and planning), we also combined the former and latter categories and examined stages of change as a dichotomous variable. Time was included as a fixed factor representing the four study visits with the last visit as the referent group.

We built a series of models including time (e.g., study visit) and stages of change. Potential confounders were identified *a priori* by examining the literature. However, because there is limited information regarding stages of change in relation to medication adherence, we also explored additional potential confounders. Each potential confounder was separately added to this base model and examined for statistical significance ($p \leq 0.05$). Since this was an exploratory analysis, each covariate found to be statistically significant when added to the base model was included in the adjusted model. Age, sex, race, educational attainment, marital status, and type of ART regimen were included in the final model regardless of

statistical significance. Age, physical and mental health (scores ranging from 0 to 100 representing the SF-12 physical and mental component scales), depression (scores ranging from 0 to 9 representing the number of depressive symptoms reported on the PC-SAD), and duration on ART (in months) were included as continuous variables. Race (Asian, Black (non-Hispanic), Hispanic, other vs. White), highest educational attainment (grade school, college, graduate/professional school vs. completion of high school), marital status (married, other, vs. single), HIV risk factors (sex with a woman, injecting drugs, other, vs. sex with a man), ART regimen type (NNRTI or NRTI vs. PI-based regimens), health status (fair/poor or good vs. very good/excellent), and length of relationship with health care provider (less than 6 months, 6 months to 1 year, 1–2 years, 3–5 years, vs. 5 years or more) were included as dummy categorical variables. Sex (female vs. male), homelessness (yes vs. no), any employment (yes vs. no), ART dosing regimen (daily vs. twice daily), health insurance status (yes vs. no), alcohol use (3–4 times per week or more frequent use vs. less frequent use), and drug use (any vs. none) were included in the model as dichotomous variables. We also examined the interaction between sex and HIV risk acquisition factor. Type-3 *p* values are presented, with 0.05 or lower indicating statistical significance.

Results

The study sample included 137 patients with 450 visits. Although 156 patients were randomized, five were excluded from this analysis because they did not have adherence data available, and an additional 14 were excluded for not having adherence data available in the 30 days following study visits. Twenty-two percent of the sample was female with a mean age of 42 years [standard deviation (SD)=7.6 years]. Nearly half of the sample was white, with 28% African-American, 20% Hispanic, and the remaining another race. Fifty-two percent had a high-school education, with 43% having college level education or beyond, and 5% a grade school education. Six percent reported homelessness or living in a shelter. About one-third of the sample was employed full-time or part-time. Seventy-two percent were enrolled in Medicaid or Mass Health. Approximately one-third reported Medicare, private health insurance, or free HIV care, respectively. Fifty-eight percent reported sex with a man as an HIV risk factor, while 13% reported sex with a woman, 14% reported injecting drugs and 15% reported other risk factors. The average time on the monitored ART was 19.1 months (SD=20), while the average duration of ART use overall was nearly 80 months (SD=60). About two-thirds of the patients had twice daily ART regimens. Approximately 40% had been with their HIV care provider for 5 years or longer (Table 1).

Across the four study visits, the majority of patients were in the action and maintenance phases. The proportion of patients classified as pre-contemplation at each study visit ranged from 0–1%, between 4–9% for contemplation, between 6–10% for planning, between 15–31% for action, and between 49–66% for maintenance. The overall average adherence summarized across visits was 72% (SD=30). Adherence by stage of change summarized across all study visits was 14% (SD=13) in pre-contemplation, 49% (SD=35) in contemplation, 47% (SD=32) in planning, 69% (SD=29) in action, and 80% (SD=26) in maintenance, although sample sizes for

TABLE 1. BASELINE DEMOGRAPHIC, BEHAVIORAL, AND HEALTH CHARACTERISTICS OF 137 PATIENTS CURRENTLY TAKING ART WHO HAD ADHERENCE DATA AVAILABLE FOR 30 DAYS FOLLOWING STUDY VISITS

<i>Characteristic</i>	
Age (mean years, SD)	42.2 (7.6)
Female, %	21.6
Race/ethnicity, %	
White	48.1
African American	27.8
Hispanic	20.3
Other	3.8
Education, %	
Grade school	5.2
High school	51.5
College or beyond	43.3
Marital status, %	
Single	53.7
Married	9.7
Other	36.6
Homeless, % living in shelter or homeless	6.0
Employed full time, %	33.6
HIV risk factor, %	
Sex with a man	57.5
Sex with a woman	13.4
Injecting drugs	14.2
Other	14.9
Physical Component Score ^a (mean, SD)	46.0 (9.9)
Mental Component Score ^a (mean, SD)	43.4 (12.4)
Depression ^b (mean, SD)	2.7 (2.5)
ART regimen, %	
PI	44.7
NNRTI	25.8
NRTI	29.5
ART dosing regimen, %	
Once daily	36.6
Twice daily	63.4
Duration on monitored ART (mean months, SD)	19.1 (20.0)
Duration on HIV meds (mean months, SD)	79.8 (59.9)
Health status, %	
Excellent	6.7
Very good	24.6
Good	42.5
Fair	23.9
Poor	2.2
Health insurance status, %	
Medicaid	71.6
Medicare	30.6
Private/commercial	31.3
Free care	26.9
Length of relationship with current provider, %	
Less than 6 months	11.7
6 months to 1 year	10.2
1–2 years	17.5
3–5 years	16.8
More than 5 years	40.9
Drink alcohol 3–4 times a week or more frequently ^c , %	12.4
Used alcohol daily or more frequently, or used cocaine, heroin, amphetamines, Ecstasy, G, K or methadone ^c , %	35.8

ART, antiretroviral therapy; SD, standard deviation.

^aFrom the Medical Outcomes Study Short Form 12-item survey;

^bnumber of symptoms reported on the PC-SAD (Primary Care Screener for Affective Disorder); ^cmeasured at randomization.

pre-contemplation, contemplation, and planning were much lower than action and maintenance. The pre-contemplation, contemplation, and planning group included 73 study visits (16%) and the action and maintenance group was comprised of 373 study visits (84%).

Results from multivariate models appear in Table 2. Because of sample size issues, and since we would expect those in the action and maintenance phases to have more established adherence behaviors than those in the earlier stages, we grouped contemplation and planning and compared them to action and maintenance in multivariate analysis. We also dropped those in the pre-contemplation phase from this analysis ($n=2$ study visits). Results from the grouped model were similar to models including each stage separately (data not shown), in that the earlier stages (i.e., contemplation and planning) had lower adherence compared to the action and maintenance stages. In crude models, contemplation and planning stages of change were associated with adherence scores in the next 30 days approximately 10% lower than those in the action and maintenance stages, an association which persisted following adjustment for potential confounders [adjusted estimated difference = -9.8 , standard error (SE) = 4.5 , $p=0.04$].

While the associations between adherence and the interaction between HIV risk factors and sex, employment, physical and mental functioning, and depression were statistically significant ($p \leq 0.05$) in crude models, only the interaction between HIV acquisition category and sex remained statistically significant after adjusting for all other potential confounders. Compared to males who reported sex with men as an HIV acquisition risk, both females and males with unknown risk, males having sex with women, and males injecting drugs all had significantly lower medication adherence in the next 30 days ($p=0.04$). The largest differences in adherence were seen among those with unknown HIV risk factors (adjusted estimated difference = -14.8 ,

SE = 8.0 for females and estimated difference = -29.1 , SE = 7.6 for males).

Discussion

The results of this study demonstrated that classification into the earlier stages of change (i.e., pre-contemplation, contemplation, and planning) was associated with significantly lower adherence scores when compared with more progressed stage-of-change classification (i.e., action and maintenance). Willey et al. studied patients attending an HIV specialty clinic in 1994 and found that 15.2% of patients prescribed ART were in pre-contemplation, contemplation, and planning stages, and we found a strikingly similar rate of 17% 10 years later among patients enrolled in a clinical trial.⁶ This study extends this earlier work by including more patients, following them over time, and adjusting for possible confounders in multivariable models. Similar findings have been observed for other chronic conditions, including depression.¹¹

These results from a clinical trial support the assertion that a sizable minority of patients who agree to take ART are not yet ready to do so. Trial entry criteria included a recent detectable HIV-RNA measurement, so our findings may not be broadly generalizable to all patients currently taking ART, but the underlying principle is important for HIV care providers to understand. Patients in earlier phases of the stages of change may not have been committed to taking ART when they initiated treatment, or they may have "relapsed," or cycled out of the action/maintenance phase at some point during their treatment history. In any event, prescribers of ART should be aware that some patients believed to be established on ART are probably non-adherent for reasons that go beyond forgetfulness, which has important implications for counseling. While those in action and maintenance stages may benefit from rewards and reminders,¹²⁻¹⁴ those in earlier

TABLE 2. ESTIMATES, STANDARD ERRORS, AND P VALUES FROM REPEATED MEASURES ANCOVA CRUDE AND ADJUSTED MODELS^a OF ADHERENCE IN 30 DAYS FOLLOWING STUDY VISITS AMONG 137 PATIENTS (WITH 450 VISITS) CURRENTLY TAKING ANTIRETROVIRAL THERAPY (ART)

	Crude models		Adjusted model	
	Estimate	SE	Estimate	SE
Stage of change (contemplation/ planning vs. action/maintenance)	-10.7	4.5	-9.8	4.5
Sex and HIV risk ^b				
Male, sex with men	REF		REF	
Female, sex with men	-2.2	6.4	3.8	7.1
Female, not sure/other risk	-8.1	7.0	-5.7	9.1
Male, sex with women	-19.0	6.4	-14.8	8.0
Male, injecting drugs	-17.4	8.4	-12.0	8.8
Male, not sure/other risk	-32.3	7.7	-29.1	7.6
Unemployed (vs. working full/part time)	-11.5	4.5	-7.8	5.2
Physical component score (SF-12)	0.7	0.2	0.4	0.2
Mental component score (SF-12)	0.4	0.2	0.4	0.2
Depressive symptoms (PC-SAD)	-2.0	1.0	0.5	1.2

Bold typeface indicates statistical significance ($p \leq 0.05$). SF-12: Medical Outcomes Study Short Form 12-item survey; PC-SAD: Primary Care Screener for Affective Disorder.

^aCrude models included stage of change, study visit, and each factor separately. The adjusted model included all variables presented in the table, plus study visit, age, sex, race, educational attainment, marital status, and type of ART regimen (PI, NNRTI or NRTI). ^bNo females reported injecting drugs, so this category was not included.

stages, who are not fully engaged in treatment, may be more likely to benefit from counseling that focuses on the pros and cons of treatment,^{4,15,16} correcting possible misconceptions about the therapy, and addressing the underlying issues that are preventing them from fully engaging in care.

A criticism of the stages of change model is that it does not capture changes in the many facets and dimensions of behaviors required for complex behavior change.¹⁷ For example, medication adherence requires many different behaviors beyond swallowing a pill, including retention to provider visits, filling prescriptions, and consistently taking doses,¹⁸ and it is unclear to which of these many behaviors the stages of change are targeted. This criticism notwithstanding, in this study assessing stage of change—which can be done quickly and easily—clearly identified patients at higher risk of objectively measured non-adherence. Additional research focused on the specific pros and cons of adherence associated with different stages of change may help elucidate the mechanisms that underlie this complex behavior change.

Tools for clinicians to assess patients' engagement and commitment to adherence behaviors are greatly needed given that clinicians tend to perform poorly at predicting patients' adherence to medications.^{2,19} Research has also consistently demonstrated that demographic and other characteristics are also poor predictors of adherence behaviors.²⁰ The findings presented here support the idea that clinicians should not rely on demographic factors to predict patients' adherence, as none were associated with adherence. Additional research is needed to test the use of the stages of change as a screening tool in clinical settings.

It is interesting to note that HIV acquisition risk factor was the only other statistically significant predictor of medication adherence beyond stages of change. Previous research has shown that high-risk behaviors may be associated with adherence to ART,^{21,22} however, the relationship is not entirely consistent.²³ Previous research has focused primarily on changes in risk behaviors following use of ART.²⁴ It is important to note that the assessment of HIV risk transmission category in this study occurred at baseline and may refer to behaviors, such as injecting drugs, no longer practiced by patients. In addition, we did not account for risk reduction behaviors in this analysis, such as condom use or sharing of needles, and therefore cannot make any statements about how these risk profiles may interact with medication adherence to impact transmission. In the current study both males and females with unknown risk factors demonstrated the lowest medication adherence, and it is likely that this measure is a proxy for other known predictors of poor adherence, such as stressful life events, lack of social support, and other psychosocial factors.²⁰

The current study has several limitations. First, the assessment of stages of change may be subject to social desirability bias resulting in misclassification of the exposure of interest. This would lead to an underestimate of those in early stages of change and would potentially dilute the association between stage of change and adherence towards the null. We did not assess the impact of side effects, a factor that is important in explaining adherence to ART^{20,25,26} and may be important in explaining stages of change. Electronic monitoring of medication taking is not a perfect measurement tool, and some measurement error is likely present.²⁷ For example, there is no guarantee that a patient opening the cap actually

took the medication as directed. If patients systematically open their medication bottles without taking the drug, adherence may be overestimated. Our findings may not be generalizable beyond the greater New England area; however, sampling from patients currently in care across a wide variety of clinical practices potentially increased the external validity of the current study. Finally, as noted previously, we studied patients in a clinical trial who were selected because there was some prior evidence of non-adherence, and rates of non-adherence are probably higher in unselected treatment populations.

In conclusion, in this trial setting we found that approximately 1 in 6 patients currently taking ART were in precontemplation, contemplation, or planning—not in action or maintenance—phases. ART prescribers should be aware that a sizable minority of patients taking ART either were never, or are no longer, fully engaged in treatment. Counseling and problem-solving for such patients should focus on the benefits of treatment and the root causes of non-adherence, rather than on reminder strategies. Studies that test stage of change assessment as a part of a screening strategy to detect non-adherence, or risk of non-adherence, are indicated.

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References

1. Bangsberg DR, Perry S, Charlebois ED, et al. Non-adherence to highly active antiretroviral therapy predicts progression to AIDS. *AIDS* 2001;15:1181–1183.
2. Miller LG, Liu H, Hays RD, et al. How well do clinicians estimate patients' adherence to combination antiretroviral therapy? *J Gen Intern Med* 2002;17:1–11.
3. DiClemente CC, Prochaska JO, Fairhurst SK, Velicer WF, Velasquez MM, Rossi JS. The process of smoking cessation: An analysis of precontemplation, contemplation, and preparation stages of change. *J Consult Clin Psychol* 1991;59:295–304.
4. Willey C. Behavior-changing methods for improving adherence to medication. *Curr Hypertens Rep* 1999;1:477–481.
5. Prochaska JO, Velicer WF. The transtheoretical model of health behavior change. *Am J Health Promot* 1997;12:38–48.
6. Willey C, Redding C, Stafford J, et al. Stages of change for adherence with medication regimens for chronic disease: Development and validation of a measure. *Clin Ther* 2000;22:858–871.
7. Highstein GR, Willey C, Mundy LM. Development of stage of readiness and decisional balance instruments: Tools to enhance clinical decision-making for adherence to antiretroviral therapy. *AIDS Behav* 2006;10:563–573.
8. Wilson IB, Laws MB, Safren SA, et al. Provider-focused intervention increases adherence-related dialogue but does not improve antiretroviral therapy adherence in persons with HIV. *J Acquir Immune Defic Syndr* 2010;53:338–347.

9. Ware JJr, Kosinski M, Keller SD. A 12-item short-form health survey: Construction of scales and preliminary tests of reliability and validity. *Med Care* 1996;34:220–233.
10. Rogers WH, Wilson IB, Bungay KM, Cynn DJ, Adler DA. Assessing the performance of a new depression screener for primary care (PC-SAD). *J Clin Epidemiol* 2002;55:164–175.
11. Tamburrino MB, Nagel RW, Chahal MK, Lynch DJ. Antidepressant medication adherence: A study of primary care patients. *J Clin Psychiatry* 2009;11:205–211.
12. Haynes RB, Ackloo E, Sahota N, McDonald HP, Yao X. Interventions for enhancing medication adherence. *Cochrane Database Syst Rev*. 2008; CD000011.
13. Galarraga O, Genberg BL, Martin RA, Barton Laws M, Wilson IB. Conditional economic incentives to improve HIV treatment adherence: Literature review and theoretical considerations. *AIDS Behav* 2013;17:2283–2292.
14. Defulio A, Silverman K. The use of incentives to reinforce medication adherence. *Prev Med* 2012;55:S86–S94.
15. Velicer WF, Prochaska JO, Bellis JM, et al. An expert system intervention for smoking cessation. *Addict Behav* 1993;18:269–290.
16. Willey C, Laforge R, Blais L, Pallonen U, Prochaska J, Botelho R. Public health and the science of behavior change. *Curr Issues Public Health* 1996;2:18–25.
17. Brug J, Conner M, Harre N, Kremers S, McKellar S, Whitelaw S. The transtheoretical model and stages of change: A critique: Observations by five commentators on the paper by Adams, J. and White, M. (2004) Why don't stage-based activity promotion interventions work? *Health Educ Res* 2005;20:244–258.
18. Steiner JF. Rethinking adherence. *Ann Intern Med* 2012;157:580–585.
19. Paterson DL, Swindells S, Mohr J, et al. Adherence to protease inhibitor therapy and outcomes in patients with HIV infection. *Ann Intern Med* 2000;133:21–30.
20. Ammassari A, Trotta MP, Murri R, et al. Correlates and predictors of adherence to highly active antiretroviral therapy: Overview of published literature. *J Acquir Immune Defic Syndr* 2002;31:S123–S127.
21. Flaks RC, Burman WJ, Gourley PJ, Rietmeijer CA, Cohn DL. HIV transmission risk behavior and its relation to antiretroviral treatment adherence. *Sex Transm Dis*. 2003;30:399–404.
22. Kalichman SC, Cherry C, Amaral CM, et al. Adherence to antiretroviral therapy and HIV transmission risks: Implications for test-and-treat approaches to HIV prevention. *AIDS Patient Care STDS* 2010;24:271–277.
23. Diamond C, Richardson JL, Milam J, et al. Use of and adherence to antiretroviral therapy is associated with decreased sexual risk behavior in HIV clinic patients. *J Acquir Immune Defic Syndr* 2005;39:211–218.
24. Sethi AK, Celentano DD, Gange SJ, Gallant JE, Vlahov D, Farzadegan H. High-risk behavior and potential transmission of drug-resistant HIV among injection drug users. *J Acquir Immune Defic Syndr* 2004;35:503–510.
25. Ammassari A, Murri R, Pezzotti P, et al. Self-reported symptoms and medication side effects influence adherence to highly active antiretroviral therapy in persons with HIV infection. *J Acquir Immune Defic Syndr* 2001;28:445–449.
26. Roberts KJ, Mann T. Barriers to antiretroviral medication adherence in HIV-infected women. *AIDS Care* 2000;12:377–386.
27. Wendel CS, Mohler MJ, Kroesen K, Ampel NM, Gifford AL, Coons SJ. Barriers to use of electronic adherence monitoring in an HIV clinic. *Ann Pharmacother*. 2001;35:1010–1015.

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